# Oral Sessions
# Haemodynamic optimization: 0822–0826

## 0822

### EARLY LACTATE-DIRECTED THERAPY IN CRITICALLY ILL PATIENTS ADMITTED TO THE INTENSIVE CARE: A RANDOMIZED CONTROLLED MULTI-CENTRE TRIAL

T. Jansen[1], J. Van Bommel[1], J. Schoonderbeek[2], S. Sleeswijk Visser[3], J. Van der Klooster[4], A. Lima[1], S. Willemsen[5], J. Bakker[1], LACTATE Study Group

[1]Erasmus Medical Center, Intensive Care Medicine, Rotterdam, Netherlands, [2]Ikazia Hospital, Intensive Care Medicine, Rotterdam, Netherlands, [3]Reinier de Graaf Hospital, Intensive Care Unit, Delft, Netherlands, [4]Sint Franciscus Gasthuis, Intensive Care Medicine, Rotterdam, Netherlands, [5]Erasmus Medical Center, Biostatistics, Rotterdam, Netherlands

**INTRODUCTION.** Hyperlactatemia in critically ill patients is associated with increased mortality. However, it is unknown whether the use of lactate clearance as a resuscitation endpoint improves survival.

**OBJECTIVE.** The primary objective of this multi-centre study was to assess the effect of lactate-directed therapy on hospital mortality, in patients admitted to the ICU with a lactate level of ≥3.0 mmol/l.

**METHODS.** We randomly allocated patients with hyperlactatemia to either lactate-directed therapy or non-lactate directed therapy during the first 8 h of ICU stay. Hospital mortality (primary outcome), resuscitation endpoints, administered therapy, organ failure and use of health care resources were compared between the two groups.

**RESULTS.** In the intention-to-treat population of 348 patients, early lactate-directed therapy did not significantly reduce in-hospital mortality as compared with non-lactate directed therapy (33.9% vs. 43.5%, $p = 0.067$). However, when corrected for predefined risk factors, hospital mortality was lower in patients assigned to early lactate-directed therapy (hazard ratio 0.61, 95% CI 0.43–0.87, $p = 0.006$). Additionally, early lactate-directed therapy resulted in a lower SOFA score between 9 and 72 h, earlier discharge from the ICU, earlier weaning from mechanical ventilation and earlier cessation of inotropes.

**CONCLUSION.** The use of lactate-directed therapy in the initial resuscitation of critically ill patients admitted to the ICU with increased blood lactate levels reduces hospital mortality in an intention-to-treat analysis corrected for predefined risk factors. In addition lactate-directed therapy significantly decreases organ failure and the use of health care resources in these patients.

**TRIAL REGISTRATION**. ClinicalTrial.gov number NCT00270673.

## 0823

### A RANDOMISED CONTROLLED TRIAL OF THE EFFECTS OF POST-OPERATIVE HAEMODYNAMIC OPTIMISATION ON MICROVASCULAR FLOW, TISSUE OXYGENATION AND INFLAMMATORY MARKERS AFTER MAJOR ABDOMINAL SURGERY

S. Jhanji[1], A. Vivian-Smith[1], S. Lucena-Amaro[1], D. Watson[1], C. J. Hinds[1], R. M. Pearse[1]

[1]Barts and The London School of Medicine and Dentistry, William Harvey Research Institute, London, United Kingdom

**INTRODUCTION.** Perioperative Goal Directed Haemodynamic Therapy (GDHT) appears to improve outcome [1]. Importantly, the biological mechanisms underlying these beneficial effects have not been investigated.

**OBJECTIVES.** To assess the effects of three haemodynamic regimens on tissue microvascular flow and oxygenation in patients after major abdominal surgery.

**METHODS.** Approval from the local ethics committee and the competent authority were granted. Patients were randomised to receive one of three haemodynamic protocols for 8 h immediately after major abdominal surgery. The central venous pressure (CVP) group received intravenous (iv) colloid boluses to achieve a sustained rise in CVP. The stroke volume (SV) group received iv colloid boluses to achieve a sustained rise in SV. In the SV plus dopexamine group, patients received iv colloid boluses to achieve a sustained rise in SV plus a fixed rate infusion of dopexamine (0.5 μg/kg/min). Data collected included oxygen delivery index ($DO_2I$) (lithium dilution & pulse power analysis), mean arterial pressure (MAP), sublingual microvascular flow videos (sidestream darkfield imaging), cutaneous microvascular flow (laser Doppler), cutaneous tissue $PtO_2$ (Clark electrode) and serum levels of Il-1$\beta$, Il-6, Il-8, TNF-$\alpha$ and ICAM-1. Data are presented as mean (SD) or median (IQR). *$p < 0.05$, **$p < 0.01$ over time. †$p < 0.05$, ‡$p < 0.01$ vs CVP group.

**RESULTS.** 135 patients were recruited. SV guided fluid therapy with dopexamine was associated with a significant increase in $DO_2I$, $ScvO_2$, sublingual and cutaneous microvascular flow and tissue $PtO_2$ but no difference in serum inflammatory markers. There were no siginificant differences in morbidity, mortality or hospital stay (Tables 1, 2, 3).

**TABLE 1** PATIENT DEMOGRAPHICS AND OUTCOMES

| | CVP group | SV group | SV plus dopexamine group |
|---|---|---|---|
| *n* | 45 | 45 | 45 |
| Age (years) | 70 (64–78) | 68 (59–77) | 65 (59–74) |
| P-POSSUM | 40 (34–44) | 35 (31–40) | 34 (31–40) |
| Complications (*n* [%]) | 30 (67%) | 26 (58%) | 31 (69%) |
| Hospital stay (days) | 15 (10–26) | 14 (11–26) | 16 (11–28) |
| Hospital mortality (*n* [%]) | 6 (13%) | 5 (11%) | 4 (9%) |

| | CVP group | SV group | SV plus dopexamine group |
|---|---|---|---|
| MAP hour 0 (mmHg) | 80 (22) | 76 (15) | 80 (18) |
| MAP hour 8 (mmHg) | 77 (14) | 77 (14) | 74 (12) ** |
| $DO_2I$ hour 0 (ml/min/m$^2$) | 477 (146) | 449 (145) | 498 (157) |
| $DO_2I$ hour 8 (ml/min/m$^2$) | 467 (159) | 484 (150)*† | 614 (209)**‡ |
| $ScvO_2$ hour 0 (%) | 73 (10) | 73 (7) | 70 (11) |
| $ScvO_2$ hour 8 (%) | 73 (7) | 74 (6) | 78 (8)**† |

* $p < 0.05$, ** $p < 0.01$ over time. † $p < 0.05$, ‡ $p < 0.01$ vs CVP group

| | CVP group | SV group | SV plus dopexamine group |
|---|---|---|---|
| Change in sublingual perfused vessel density during intervention (n/mm) | −0.8 (1.7) | +0.1 (2.0) | +0.5 (2.5)† |
| Change in cutaneous reactive hyperaemia ratio during intervention | −0.7 (1.3) | 0.0 (2.3) | +1.4 (2.7)‡ |
| Change in $PtO_2$ during intervention (kPa) | 0.0 (2.9) | +0.5 (3.4) | +1.7 (3.7)† |

† $p < 0.05$, ‡ $p < 0.01$ vs CVP group

**CONCLUSIONS.** Post-operative GDHT with dopexamine improves global haemodynamics, tissue microvascular flow and oxygenation. Systemic inflammatory markers were unchanged.

**REFERENCES.** 1. Pearse et al (2005) Crit Care 9:R687–R693
2. Jhanji et al (2009) Intensive Care Med 35:671–677

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## 0824

### INVERSE CORRELATION BETWEEN NITROGLYCERIN-INDUCED CHANGES IN CENTRAL-PERIPHERAL TEMPERATURE GRADIENT AND CHANGES IN SUBLINGUAL PERFUSED CAPILLARY DENSITY IN PATIENTS WITH CARDIOGENIC SHOCK OR END-STAGE CHRONIC HEART FAILURE

C. den Uil[1], W. Lagrand[2], M. van der Ent[1], L. Jewbali[1], P. Spronk[3], M. Simoons[1]

[1]Erasmus Medical Center, Rotterdam, Netherlands, [2]Academic Medical Center at the University of Amsterdam, Amsterdam, Netherlands, [3]Gelre Hospitals, Apeldoorn, Netherlands

**OBJECTIVE.** To investigate the correlation between nitroglycerin-induced changes in central-peripheral temperature gradient and changes in sublingual perfused capillary density in patients with cardiogenic shock or end-stage chronic heart failure.

**METHODS.** A nitroglycerin dose-response study was performed in fifteen patients with cardiogenic shock ($n = 9$) or end-stage chronic heart failure ($n = 6$) admitted to Erasmus University Medical Center. We did hemodynamic measurements at baseline and during increasing infusion rates of nitroglycerin (up to a maximum dose of 133 μg min$^{-1}$). As parameters of tissue perfusion, we measured central-peripheral temperature gradient (delta-T) and sublingual perfused capillary density (PCD). Sublingual PCD was measured with SDF imaging and AVA 3.0 software. Capillaries were defined as micro-vessels with a diameter of <20 μm. We pooled all nitroglycerin-induced changes in delta-T and PCD.

**RESULTS.** Nitroglycerin dose-dependently decreased mean arterial pressure ($p = 0.01$), cardiac filling pressures (central venous pressure: $p < 0.001$; pulmonary capillary wedge pressure: $p = 0.001$), and mixed-venous oxygen saturation ($p = 0.02$). Nitroglycerin decreased delta-T ($p < 0.001$) and improved sublingual PCD ($p < 0.001$). Macro-hemodynamic and microcirculatory responses to nitroglycerin infusion were consistent in patients with either cardiogenic shock or end-stage chronic heart failure. A significant correlation was found between pooled changes in both parameters of tissue perfusion (Spearman $r = -0.48$, $p < 0.001$; Fig. 1).

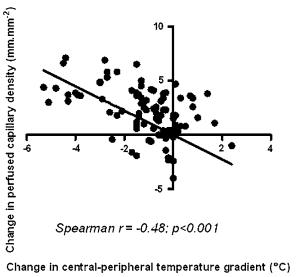


**Fig. 1**

**CONCLUSIONS.** Nitroglycerin dose-dependently increased tissue perfusion, measured by two independent parameters. There was a significant correlation between induced changes in both parameters of tissue perfusion.

## 0825

### VASOPRESSIN, EPINEPHRINE, AND CORTICOSTEROIDS FOR INHOSPITAL CARDIAC ARREST [NCT00729794]

S. D. Mentzelopoulos[1], G. Chamos[1], T. Taidou[1], D. Konstantopoulos[2], A. Lomaka[2], V. Mintzi[3], E. Sika[3], G. Ganeli[3], K. Koutsodimou[3], D. Makris[4], S. Sourlas[5]

[1]University of Athens, Intensive Care Medicine, Athens, Greece, [2]Evaggelismos Hospital, Department of Anesthesiology, Athens, Greece, [3]University of Larissa, Anesthesiology, Larissa, Greece, [4]University of Larissa, Intensive Care Medicine, Larissa, Greece, [5]401 General Army Hospital Athens, Anesthesiology and Intensive Care Medicine, Agia Paraskevi, Greece

**INTRODUCTION.** The addition of vasopressin during cardiopulmonary resuscitation (CPR) and of steroids during and after CPR may increase the rates of return of spontaneous circulation (ROSC) and improve post-arrest survival [1]. We seek to provide definitive evidence supporting this hypothesis and its generalizability by adequately increasing the size of the originally studied population [1] in the context of a three-center, randomized, controlled trial. Herein, we report the results of the second interim analysis.

**METHODS.** Adult in-patients with cardiac arrest were randomized to receive either (1) vasopressin (20 IU/CPR cycle for 5 cycles) plus epinephrine (1 mg/CPR cycle) plus methylprednisolone (single dose = 40 mg on the first CPR cycle) (study group); or (2) placebo plus epinephrine plus placebo (control group). Following return of spontaneous circulation (ROSC), study group patients with postresuscitation shock also received stress dose hydrocortisone (300 mg/day for 3–7 days and then gradual taper), whereas controls received placebo. Primary endpoints were ROSC for at least 15 min, and survival to discharge either to home or to a rehabilitation facility.

**RESULTS.** Data from 180 patients were analyzed. Patient clinical profiles were similar. Study group patients vs. controls had higher mean arterial pressure during and after CPR [mean (SD), 75.1 (21.9) vs. 50.4 (13.0) mm Hg and 94.3 (37.2) vs. 70.7 (22.2) mm Hg, $p < 0.001$], and higher rates of ROSC (71/85 vs. 55/95, $p < 0.001$) and discharge to either home or a rehabilitation/high dependency unit (15/85 vs. 5/95, $p = 0.009$).

**CONCLUSION.** These results indicate improved study group survival. The study is continued according to an interim analysis stopping rule of adjusted $p < 0.001$.

**GRANT ACKNOWLEDGEMENT.** Supported in part by the Thorax Foundation.

**REFERENCE.** 1. Mentzelopoulos SD et al. (2009) Arch Intern Med 169:15–24

## 0826

### COMBINATION OF STATIC AND FUNCTIONAL PRELOAD PARAMETERS ENABLES EARLY DETECTION OF RIGHT VENTRICULAR FAILURE

H. P. Richter[1], D. A. Reuter[1], C. Petersen[1], A. E. Goetz[1], J. C. Kubitz[1]

[1]University Medical Center Hamburg-Eppendorf, Department of Anaesthesiology, Hamburg, Germany

**AIMS.** Diagnosis of right ventricular dysfunction (RVD) or failure is often delayed or missed. In case of RVD, optimization of cardiac preload is essential for providing hemodynamic stability. So far, static right ventricular (RV) preload parameters such as central venous pressure (CVP) or RV end-diastolic volume (RVEDV) are used to assess cardiac preload in RVD. As the interdependence of RV and left ventricular (LV) function is supposed to be reflected in the relationship of RV and LV preload parameters, we now investigated in an experimental model whether the combination static RV and functional LV preload parameters can be used for early detection of RVD and for guidance of volume therapy.

**METHODS.** After approval by the local governmental commission, fifteen anesthetized pigs (29 ± 0.8 kg) were examined. CVP, RV end-diastolic pressure (RVEDP) and mean arterial pressure (MAP) were recorded using micro-tip catheters. Mean pulmonary artery pressure (MPAP) and RVEDV were measured by a thermodilution pulmonary artery catheter (VOLEF, Pulsion, Germany). Pulse pressure variation (PPV) and stroke volume variation (SVV) (derived from an ultrasonic flowprobe on the ascending aorta) were calculated over 5 respiratory cycles. Cardiac output (CO) was derived from a pulmonary artery flowprobe. After a *baseline* measurement, *RVD* was induced by increasing MPAP by 50% by continuous infusion of the thromboxan-analogon U46619. Then, 300 ml blood were extracted (*vol.extraction*), followed by a volume challenge (600 ml) (*vol.challenge)*.

**RESULTS.** The increase in RV afterload resulted in a reduction of MAP and CO. CVP, SVV and PPV increased, while heart rate (HR), RVEDP and RVEDV remained unchanged. Volume extraction decreased MAP, MPAP, CVP and RVEDP without changes in SVV or PPV. During the volume challenge, MAP, MPAP, CVP, RVEDP and RVEDV increased again, without significant changes in CO, SVV or PPV.

**TABLE 1** RESULTS

| | Baseline | RVD | Vol. extraction | Vol. challenge |
|---|---|---|---|---|
| HR (beats/min) | 96 (15) | 98 (16) | 100 (19) | 100 (15) |
| MPAP (mmHg) | 25.1 (3.3) | 37.4 (4.9)** | 34.1 (6.4)† | 41.8 (7.8)# |
| MAP (mmHg) | 72.2 (14.1) | 60.1 (11.3)** | 53.2 (10.6)† | 63.7 (9.1)# |
| CO (l/min) | 2.8 (0.6) | 2.3 (0.7)** | 2.1 ± (0.7) | 2.3 ± (0.6) |
| CVP (mmHg) | 11.3 (4.6) | 12.6 (4.7)* | 10.3 (4.7)† | 14.8 (6.0)# |
| RVEDP (mmHg) | 13.8 (4.6) | 14.7 (5.8) | 11.4 (4.9)† | 16.6 (3.6)# |
| RVEDV (ml) | 112 (27) | 110 (19) | 108 (23) | 124 (19)# |
| SVV (%) | 11 (3) | 14 (4)* | 14 (5) | 13 (4) |
| PPV (%) | 13 (4) | 17 (6)* | 16(7) | 15 (5) |

Mean values (standard deviation) are presented; * $p < 0.05$ vs. baseline;
** $p < 0.001$ vs. baseline; † $p < 0.001$ vs. RVD; # $p < 0.05$ vs. vol.extraction

**CONCLUSIONS.** A simultaneous increase in both static RV (CVP) and functional LV preload parameters (SVV, PPV) seems indicative for RVD. Further diagnosis is warranted. Continuous registration of CVP and SVV or PPV may provide an early indicator of RVD and help to guide volume therapy in RVD.

# Acute lung injury: Pathophysiology: 0827–0831

## 0827

### THE SELECTIVE α7NACHR AGONIST GTS-21 ATTENUATES VENTILATOR-INDUCED INFLAMMATION AND LUNG INJURY

M. Kox[1], J.C. Pompe[1], M. Vaneker[2], L.M. Heunks[1], J. G. van der Hoeven[1], C. W. Hoedemaekers[1], P. Pickkers[1]

[1]Radboud University Nijmegen Medical Centre, Intensive Care Medicine, Nijmegen, Netherlands, [2]Radboud University Nijmegen Medical Centre, Anesthesiology, Nijmegen, Netherlands

**INTRODUCTION.** Mechanical ventilation (MV) induces an inflammatory response that contributes to lung injury such as in ALI or ARDS. The efferent vagus nerve can limit the inflammatory response via the α7 nicotinic acetylcholine receptor (α7nAChR), the so-called cholinergic anti-inflammatory pathway. The aim of this study was to evaluate the effect of the selective α7nAChR agonist GTS-21 on pulmonary and systemic inflammation and lung injury induced by MV using clinically relevant ventilator settings.

**METHODS.** C57BL6 mice ($n = 40$) were i.p. injected with 8 mg/kg GTS-21 or placebo after which they were mechanically ventilated for 4 h (tidal volume 8 ml/kg; PEEP 1.5 cm $H_2O$; $FiO_2$ 0.45). Untreated, not mechanically ventilated mice were used as controls. Mean arterial pressure (MAP) and rectal temperature were monitored throughout the ventilation period. Arterial blood gases were obtained at the end of the experiment and TNF-α, IL-6, IL-1α, IL-1β, KC and IL-10 were determined in plasma and lung homogenates. Lung TNF-α and IL-10 mRNA expression was measured in lung homogenates using quantitative PCR.

**RESULTS.** MAP and rectal temperature did not differ between GTS-21 and placebo-treated animals. In GTS-21-treated mice, the alveolar-arterial (A-A) gradient after MV was significantly reduced compared to placebo (18.7 ± 0.8 vs. 20.8 ± 0.6 kPa; $p = 0.04$). MV resulted in an increase of all cytokines in plasma and lung compared to control mice. TNF-α was significantly lower in plasma of GTS-21-treated animals compared to placebo (196.2 ± 50.8 vs. 331.9 ± 31.9 pg/ml; $p = 0.04$). Similarly, in lung homogenates a distinct trend was observed towards lower TNF-α levels in GTS-21-treated mice (53.9 ± 12.5 vs. 79.1 ± 5.6 pg/mg protein; $p = 0.06$). IL-10 levels were unaffected by GTS-21. MV strongly increased TNF-α mRNA expression in lungs of placebo animals (21-fold compared to controls), this was significantly lower in GTS-21-treated mice (12-fold compared to controls; $p = 0.02$). IL-10 mRNA expression was similar in GTS-21-treated and placebo animals.

**CONCLUSION.** MV with clinically relevant ventilator settings results in activation of the immune system. GTS-21 inhibits pro-inflammatory cytokine production while not affecting the anti-inflammatory cytokine IL-10.The reduced A-A gradient in GTS-21-treated animals indicates attenuation of lung injury. In conclusion, limiting the inflammatory response appears to reduce lung injury and therefore the cholinergic anti-inflammatory pathway may represent new treatment options for MV-induced lung injury.

## 0828

### PHOSPHOINOSITIDE 3 KINASE BETA ATTENUATES INFLAMMATION AND FIBROSIS IN A BLEOMYCIN MODEL OF ACUTE LUNG INJURY

V. Fanelli[1], E. Ciraolo[2], M. Bosco[3], L. Delsedime[3], A. Mensa[1], E.L. Martin[1], L. Delsorbo[1], B. Assenzio[1], M. L. Campanari[1], E. Hirsch[2], V. M. Ranieri[1]

[1]Università di Torino, Dept. of Anaesthesiology and Critical Care Medicine, Torino, Italy, [2]Università di Torino, Department of Genetics, Biology and Biochemistry, Torino, Italy, [3]Università di Torino, Dept Biomedical Sciences and Human Oncology, Torino, Italy

**INTRODUCTION.** Aberrant wound-healing responses to injury leading to lung fibrosis contribute to the pathogenesis of ARDS and are associated with high morbidity and mortality. Lung inflammation and collagen deposition are caused by leukocytes and fibroblasts migrating into fibrin rich exudates. Class IA of the phosphoinositide 3 kinase family are mainly activated by receptor tyrosine kinases and form heterodimers composed of a catalytic subunit (p110α, β and δ) and an adaptor protein. Previous studies suggested a role of p110β in platelet aggregation, cellular migration and epithelial mesenchymal transition, which are involved in the pathogenesis of lung fibrosis. The aim of this study was to investigate the role of p110β in an animal model of lung injury.

**METHODS.** Wild type (WT) and kinase dead (KR) mice, expressing a catalytically inactive form of p110β were used. Lung injury was induced by intratracheal instillation of bleomycin sulphate (3 UI/kg), while control mice received only saline vehicle instillation. Following 14 days the severity of fibrosis and lung inflammation (Hematoxylin-Eosin and Sirius red), BALF proteins content, and synthesis of procollagen and fibronectin (RT PCR) were assessed.

Data are expressed as mean ± SEM.

**RESULTS.** See Table 1. * $p < 0.05$ KR bleo vs WT bleo; ° KR and WT bleo vs KR and WT saline; § KR saline vs WT saline.

**TABLE 1**

| | WT saline | KR saline | WT bleo | KR bleo |
|---|---|---|---|---|
| Histological lung fibrosis (arbitrary units) | 1.2 ± 0.2 | 1.5 ± 0.3 | 4.8 ± 0.4° | 6 ± 0.4*,° |
| Procollagen (fold increase over control) | 1 | 4.2 ± 0.5§ | 11.2 ± 1.2° | 26.5 ± 5.1*,° |
| Fibronectin (fold increase over control) | 1 | 3.7 ± 0.4§ | 13.8 ± 1.8° | 57 ± 6.6*,° |
| BALF proteins (mg/ml) | 200 ± 40 | 259 ± 41 | 628 ± 48° | 1.124 ± 213*,° |
| Histological lung inflammation (arbitrary units) | 1.2 ± 0.2 | 1 | 2.15 ± 0.12° | 2.78 ± 0.15*,° |

**CONCLUSION.** Compared to wild type PI3K β kinase dead mice had more lung fibrosis, altered vascular permeability and lung inflammation.

We provide the first evidence for the crucial role of PI3K β kinase activity in tissue injury repair and lung inflammation.

## 0829

### THE ANGIOPOIETINS HAVE OPPOSING EFFECTS ON THE SENSITIVITY OF HUMAN PULMONARY MICROVASCULAR ENDOTHELIAL CELLS TO MEDIATOR-INDUCED, BUT NOT TO BASAL PERMEABILITY

M. van der Heijden[1,2], G. P. van Nieuw Amerongen[2], V. W. van Hinsbergh[2], A. B. Groeneveld[1]

[1]VU University Medical Center, Intensive Care, Amsterdam, Netherlands, [2]VU University Medical Center, Physiology, Amsterdam, Netherlands

**INTRODUCTION.** Endothelial activation by host-derived mediators, such as thrombin, is central in the pathogenesis of pulmonary permeability during acute lung injury (ALI). Novel mediators that may be involved include the Tie2 receptor ligands angiopoietin-1 (Ang-1) and angiopoietin-2 (Ang-2), since plasma Ang-2 and the Ang-2/Ang-1 ratio were associated with pulmonary permeability and severity of ALI in critically ill patients. Experiments in human pulmonary microvascular endothelial cells (HPMVECs) specifically could further contribute to elucidate the effects of the angiopoietins on basal and thrombin-induced permeability. We hypothesised that Ang-1 reduces and Ang-2 enhances permeability.

**OBJECTIVES.** To study the effect of Ang-1 and Ang-2 on basal and thrombin-induced permeability of HPMVECs.

**METHODS.** HPMVECs were isolated from healthy lung obtained after lobectomy for carcinoid or metastasis. The phosphorylation status of the Tie2 receptor was analysed by western blotting. The permeability of the HPMVEC monolayer was assessed by measuring the transendothelial electrical resistance (TEER). The rate at which the thrombin-induced permeability occurred and the maximum thrombin-induced permeability were analysed as indicators of the stability of cell-cell junctions and cell contractility, respectively.

**RESULTS.** The angiopoietins had opposing effects on phosphorylation of the Tie2 receptor, since Ang-1 induced a transient increase in Tie2 phosphorylation ($p < 0.05$), which was prevented by co-treatment with Ang-2 ($p < 0.05$). Surprisingly, the angiopoietins did not affect the basal barrier function of HPMVECs. Interestingly, Ang-1 reduced and Ang-2 enhanced the rate at which the thrombin-induced permeability occurred by 25 ± 11% ($p < 0.01$) and 61 ± 34% ($p < 0.05$), respectively, while they had a less pronounced effect on the maximum thrombin-induced permeability (19 ± 3% reduction by Ang-1, $p < 0.0001$ and 18 ± 10% enhancement by Ang-2, $p = 0.0874$).

**CONCLUSIONS.** Our data indicate that Ang-1 and Ang-2 do not affect the basal barrier function of human pulmonary MVECs, while they have opposing effects on the rate at which the thrombin-induced permeability occurred, more than the maximum thrombin-induced permeability. The latter suggests that angiopoietins modulate the stability of the junctions before and during thrombin-stimulation, rather than the thrombin-induced cell contractility.

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## 0830

### ROLE OF PTX3 IN LEUKOCYTE RECRUITMENT IN ACUTE PHASE IN A MURINE MODEL OF ACID ASPIRATION LUNG INJURY

V. Zambelli[1,2], M. Scanziani[1], L. Deban[3], F. Moalli[3], M. Amigoni[1], F. Fumagalli[1,2], S. Deab[1], B. Bottazzi[3], R. Latini[2], A. Mantovani[3], A. Pesenti[1]

[1]Milano-Bicocca University, Department of Experimental Medicine, Monza, Italy, [2]Istituto di Ricerche Farmacologiche Mario Negri, Cardiovascular Research, Milano, Italy, [3]Istituto Clinico Humanitas, Rozzano, Italy

**INTRODUCTION.** Pentraxins are a superfamily of acute phase proteins. The prototypic long pentraxin 3 (PTX3) is rapidly produced and released by various cell types in response to inflammatory signals. A recent prospective study showed that PTX3 is elevated in ALI and ARDS and that its levels correlate with parameters of lung injury and systemic involvement.

**OBJECTIVES.** Our aim was to determine the role of PTX3 in inflammation in a murine model of ALI in the acute phase.

**METHODS.** Mice were injected with 100 μg of human PTX3 i.v. (hPTX3 +) or sterile saline (hPTX3 −), anesthetized and ventilated (Vt 8–10 ml/kg, RR 140 $min^{-1}$, $FiO_2$ 0.21). In order to induce lung injury 2 ml/kg of HCl (pH = 1.5) was instilled intratracheally. Mice were ventilated for 10 min, then kept in an oxygenated chamber until full awakening ($FiO_2$ 0.5). To evaluate the severity of injury, animals were sacrificed after 3 h and Broncho-Alveolar Lavage (BAL) was performed and lungs were removed and stored.

**RESULTS.** 3 h after acid instillation, pre-treatment with hPTX3 allowed a significant reduction of total cell recruitment in the alveolar space; in particular, neutrophilic influx in BAL was significantly reduced compared to mice pretreated with saline. We observed the same results also in pulmonary tissue.

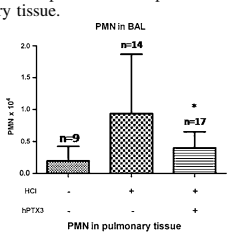


**Fig. 1** [PMN_BAL]

**Fig. 1** [PMN_tissue] *$p < 0.05$ vs *hPTX3*-

**CONCLUSIONS.** In this murine model of acid aspiration pneumonitis we showed a role of PTX3 in the initial inflammatory process, since the pre-treatment with exogenous human PTX3 reduced cellular recruitment in alveolar spaces. Thus, PTX3 might act as a intrinsic fine-regulator of initial inflammatory response, possibly limiting excessive inflammation-induced tissue damage.

## 0831

### CRITICAL ROLE OF ADENOSINE RECEPTOR A1 FOR LPS-INDUCED TRAFFICKING OF PMNS IN THE LUNG

K.-C. Ngamsri[1], R. Wagner[1], I. Vollmer[1], S. Stark[1], J. Reutershan[1]

[1]University Hospital Tübingen, Anaesthesiology and Critical Care Medicine, Tübingen, Germany

**INTRODUCTION.** Excessive transmigration of PMNs play a major role in the early development of acute lung injury (ALI). Extracellular adenosine is involved in various inflammatory pathways by signalling through four subtypes of adenosine receptors, A1, $A2_A$, $A2_B$, and A3, all members of the family of G protein-coupled receptors. A1 has particularly been implicated in leukocyte migration to inflamed tissues. However, its role in acute pulmonary inflammation remains elusive. We therefore sought to characterize the role of A1 in a model of LPS-induced migration of PMNs into the lung.

**MATERIALS AND METHODS.** In a murine model of acute lung injury, C57/Bl6 and for A1 gene deficient mice ($A1^{-/-}$) were exposed to aerosolized LPS. We used a flow cytometry-based method to quantify the accumulation of PMNs in all compartments of the lung. LPS-induced microvascular permeability was determined by the extravasation of Evans blue, and the release of inflammatory cytokines into the brochoalveolar lavage fluid (BAL) was assessed by ELISA. In addition, we tested the effects of the selective A1 agonist 2′-Me-CCPA in vitro and in vivo. To determine specific effects of A1 on hematopoietic and non-hematopoietic cells, chimeric mice were generated by transfer of bone marrow between wildtype and $A1^{-/-}$ mice.

**RESULTS.** LPS inhalation resulted in significant accumulation of PMNs in all compartments of wildtype mice. PMN recruitment into interstitium and alveolar airspace of A1 gene deficient mice was significantly higher than in wildtype mice. Pharmacological activation of A1 significantly reduced PMN migration to interstitium and alveolar airspace of wildtype but not of $A1^{-/-}$ mice. In chimeric mice that express A1 only on hematopoietic cells, PMN migration into the interstitium was significantly higher than in chimeric mice that expressed A1 only on non-hematopoeitic cells. Pharmacological activation of A1 in chimeric mice did only reduce PMN migration when A1 was expressed on hematopoietic cells. LPS-induced increase in Evans blue leakage was significantly higher in $A1^{-/-}$ compared with wild-type mice. Consistent with these results, the activation of A1 resulted in a significant decrease of microvascular permeability in wildtype mice. Pretreatment with the specific A1 agonist (1 mg/kgKG, ip.) decreased the release of the chemokines MIP-2 and TNFα into the alveolar space. In addition, pharmacological activation of A1 adenosine receptor resulted in significant decrease of the migration of human PMNs in an in vitro transmigration assay.

**CONCLUSION.** A1 plays a critical role in LPS-induced PMN transmigration and microvascular permeability in a murine model of ALI. These protective effects appear to be mediated by A1 on hematopoietic cells. Activation of A1 reduces PMN trafficking during pulmonary inflammation and maybe a promising approach to develop innovate therapeutic strategies for the treatment of ALI.

# Early diagnosis and epidemiology of AKI: 0832–0836

## 0832

### NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) IN ACUTE KIDNEY INJURY: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Haase[1], R. Bellomo[2], P. Devarajan[3], A. Haase-Fielitz[1], NGAL Meta-Analysis Investigator Group

[1]Charité-Universitätsmedizin Berlin, Campus Virchow-Klinikum, Dept of Nephrology and Intensive Care Medicine, Berlin, Germany, [2]Austin Hospital, Dept of Intensive Care, Melbourne, Australia, [3]Cincinnati Children's Hospital Medical Center, Dept of Pediatrics and Developmental Biology, Cincinnati, United States

**INTRODUCTION.** Neutrophil Gelatinase-Associated Lipocalin (NGAL) appears to be a promising biomarker for the early diagnosis of acute kidney injury (AKI), however a wide range in its predictive value has been reported.

**OBJECTIVES.** To perform a systematic review and meta-analysis of all observational studies to determine the diagnostic and prognostic performance of NGAL and to identify potential confounders or effective modifiers of its value in AKI.

**METHODS.** We searched MEDLINE, EMBASE, CENTRAL databases and congress abstracts for studies that reported the value of NGAL to predict AKI in different clinical settings. We included observational cohort studies using custom-made standardized data-sheets sent to the authors. The primary outcome was AKI defined as creatinine increase >50% from baseline within 7 days. Secondary outcomes included renal replacement therapy (RRT) initiation and in-hospital mortality.

**RESULTS.** We analyzed data from 18 studies and 7 countries involving 2,488 patients, out of whom 452 (18.2%) developed AKI. Overall, the area-under-the-curve for the receiver-operating-characteristic (AUC-ROC) of NGAL to predict AKI was 0.812 (95% CI 0.729–0.889, $I^2 = 44.5\%$ for heterogeneity). We found a >0.1 AUC-ROC unit difference in favor of standardized platforms (AUC-ROC 0.830, $I^2 = 7.0\%$) with cut-off of >150 ng/ml compared to 'research-based' ELISA's (0.729, $I^2 = 32.6\%$). In cardiac surgery patients, the AUC-ROC of NGAL was 0.771, $I^2 = 28.8\%$, in critically ill patients 0.728, $I^2 = 17.5\%$ and after contrast infusion 0.894, $I^2 = 3.2\%$. The diagnostic value of plasma/serum NGAL (AUC-ROC 0.771, $I^2 = 21.2\%$) was similar to that of urine NGAL (AUC-ROC 0.836, $I^2 = 22.9\%$), $p = 0.72$. We identified age to be an effective modifier of NGAL value with better predictive ability in children (AUC-ROC 0.930, $I^2 = 3.5\%$) compared to adults (AUC-ROC 0.780, $I^2 = 28.5\%$); $p = 0.036$. NGAL was a useful prognostic tool with regard to the prediction of RRT initiation (AUC-ROC 0.782, $I^2 = 9.5\%$) and in-hospital mortality (AUC-ROC 0.706, $I^2 = 10.3\%$).

**CONCLUSIONS.** NGAL is of diagnostic and prognostic value for AKI and may be considered as a useful early identifier of patients at risk for randomized controlled trials of preventive and therapeutic interventions in AKI.

## 0833

### CHANGE OF PLASMA CREATININE CONCENTRATION DURING THE 6 FIRST HOURS AFTER ADMISSION TO THE INTENSIVE CARE UNIT (ICU) ALLOWS EARLY PREDICTION OF SUBSEQUENT ACUTE RENAL FAILURE

M. Skarzynski[1], D. Garot[1], E. Mercier[1], A. Legras[1], P. F. Dequin[1], D. Perrotin[1], S. Ehrmann[1]

[1]CHRU Tours, Service de Réanimation Médicale Polyvalente, Tours, France

**INTRODUCTION.** Increasing creatinine plasma concentrations are usually associated with worsening renal function. Nevertheless this supposes a constant creatinine production and distribution volume. Whereas the former may be considered true over a short time period, the volume of distribution is subject to important changes at the initial phase of resuscitation, mainly because of fluid loading. Therefore an increase of creatinine plasma concentration may not only reflect changes in renal function in this context.

**OBJECTIVES.** To evaluate if change of plasma creatinine concentration (Δ creatinine) corrected for concomitant changes in its distribution volume over the first 6 h after ICU admission could predict a subsequent worsening of acute kidney injury (AKI).

**METHODS.** Observational, prospective study in a 25-bed medical adult ICU. Inclusion criteria were: urinary catheterization and at least one of the following within 2 h of admission: systolic blood pressure ≤90 mmHg; mean arterial pressure ≤65 mmHg; fluid resuscitation greater than 1,000 ml; use of vasopressors. Exclusion criteria were dialysis before inclusion and kidney transplantation. AKI was evaluated according to the RIFLE classification. Prospectively collected data were used at H0 (time of admission), H6, H24 and Day 3 to Day 7. Worsening of AKI after H6 was defined as an increase in RIFLE classes (NoAKI < Risk < Injury < Failure) at any time during the study period after H6. Δ creatinine was evaluated uncorrected (Equation 1: [C]H6/[C]H0) and corrected for changes in creatinine distribution volume and hemodilution (Eqs. 2 and 3 respectively).

Equation 2: [[C]H6 × 0.6 × (W+ fluid balance)]/[[C]H0 × 0.6 W].

Equation 3: ([C]H6/[C]H0)/(HbH6/HbH0).

[C]H6 and [C]H0 stand for plasma creatinine concentration at H6 and H0, W for body weight; HbH6 and HbH0 for haemoglobin concentration at H6 and H0, fluid balance for difference between fluid input and output between H0 and H6.

**RESULTS.** 49 patients were included (median [25th; 75th percentile) age 62 [49; 74] years, SAPS II 41 [30; 53,]). 27 patients (55%) had worsening of AKI after H6. There was no significant difference of uncorrected Δ creatinine between patients with or without worsening AKI after H6 (0.93 [0.89; 0.98] vs 0.85 [0.81; 0.95]). When correcting Δ creatinine using Eqs. 2 or 3, patients with subsequent worsening AKI had a significantly higher corrected Δ creatinine (0.99 [0.94; 1.04] vs 0.90 [0.85; 0.99] $p = 0.02$ and 1.00 [0.90; 1.06] vs 0.89 [0.81; 0.93] $p < 0.01$ for Eqs. 2 and 3 respectively).

**CONCLUSIONS.** When correcting for resuscitation induced changes in distribution volume, small changes in plasma creatinine concentrations occurring over the first 6 h in the ICU may allow identifying patients at risk of subsequent worsening AKI.

## 0834

### NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN IS AN EARLY BIOMARKER FOR ACUTE KIDNEY INJURY IN AN ADULT ICU POPULATION

D. Cruz[1], M. de Cal[1], F. Garzotto[1], S. Gramaticopolo[2], P. Piccinni[2], C. Ronco[1]

[1]San Bortolo Hospital, Nefrology, Vicenza, Italy, [2]San Bortolo Hospital, Anesthesia and Intensive Care, Vicenza, Italy

**INTRODUCTION.** Serum creatinine is a late marker of acute kidney injury (AKI), hindering timely intervention. Plasma and urine NGAL have been shown to be useful early markers for AKI when the timing of the renal insult is known, such as post-cardiac surgery and radiocontrast nephropathy [1]. In children, NGAL both in urine and plasma is an excellent early marker of AKI with an area under the receiver operator characteristic curve (AuROC) in the range of 0.8–0.9 [2]. However, its performance in a general adult medical-surgical ICU setting has not yet been well described.

**OBJECTIVES.** The study aims at evaluating the usefulness of plasma NGAL as an early marker of AKI in an adult general ICU.

**METHOD.** This was a prospective cohort study of 307 consecutive incident patients to an adult ICU, enrolled within 24 h of ICU admission. We excluded 5 patients with ESRD, leaving 302 patients for analysis. Clinical data, including urine output and serum creatinine, were collected daily up to ICU discharge. Blood samples for NGAL were collected daily from ICU admission for up to 4 days. Plasma NGAL (pNGAL) was measured in 873 blood samples (median 3 samples/patient), using a point-of-care device (Triage NGAL, Biosite Inc, San Diego, CA).

AKI was defined using the RIFLE (Risk-Injury-Failure-Loss-Endstage renal disease) classification. RIFLEinitial refers to the patient's RIFLE class on the 1st day of AKI. Diagnostic characteristics of pNGAL were evaluated with receiver operating characteristic (ROC) curves. We defined an event as AKI occurring within 48 h of the first pNGAL measurement.

**RESULTS.** Of 302 patients, 133 (44%) developed AKI during their ICU stay. In the AKI group, 90 patients (29.8%) had AKI within 24 h of ICU admission while 43 (14.2%) developed it later during their ICU stay (range, 2nd to 45th ICU day). RIFLEinitial class was Risk in 92 patients (30.5%), Injury in 17 (5.6%) and Failure in 24 (7.9%). Fifteen patients (5%) were treated with renal replacement therapy for AKI in the ICU.

Plasma NGAL was a good diagnostic marker for AKI development within the next 48 h (Fig. 1, area under ROC 0.78, 95% CI 0.65–0.90). Using a cut-off of 150 ng/ml for pNGAL, the sensitivity was 73% and specificity was 81%.

**CONCLUSIONS.** Plasma NGAL appears to be a useful early marker for the development of AKI in a heterogenous adult ICU population, in which the timing of the renal insult is largely unknown. Plasma NGAL allows the diagnosis of AKI up to 48 h prior to a rise in serum creatinine. It is worth noting, however, that the area under ROC is slightly lower than that reported in several pediatric studies.

**REFERENCES.** 1. Ronco C (2007) N-GAL: diagnosing AKI as soon as possible. Critcal Care 11:173.

2. Zappitelli M et al (2007) Urine N-GALis an early marker of acute kidney injury in critically ill children: a prospective cohort study. Crit Care 11:R84

## 0835

### DIAGNOSTIC PERFORMANCE OF FRACTIONAL EXCRETION OF UREA IN THE EVALUATION OF CRITICALLY ILL PATIENTS WITH ACUTE KIDNEY INJURY: A MULTICENTER COHORT STUDY

M. Darmon[1], F. Vincent[2], J. Dellamonica[3], F. Schortgen[4], F. Gonzalez[2], V. Das[1], G. Bernardin[3], L. Brochard[4], Y. Cohen[2], B. Schlemmer[1]

[1]Saint-Louis University Hospital, Paris, France, [2]Avicenne University Hospital, Bobigny, France, [3]Nice University Hospital, Nice, France, [4]Henri Mondor University Hospital, Creteil, France

**INTRODUCTION.** Several factors including diuretic use and sepsis interfere with the fractional excretion of sodium (FeNa), which is used to distinguish prerenal from intrinsic acute kidney injury (AKI). These factors do not affect the fractional excretion of urea (FeUrea) [1]. However, data on the diagnostic accuracy of FeUrea are conflicting and this index has never been validated in critically-ill patients.

**METHODS.** Observational prospective multicenter study performed in three intensive care units in university hospitals. Consecutive patients, except those with obstructive AKI, admitted to the participating ICUs during a 6-month period were included in this study. AKI was defined accordingly to the AKIN definition [2]. Prerenal AKI was defined as AKI with a cause for renal hypoperfusion and reversal within 3 days. Results are reported as medians [IQR].

**RESULTS.** 203 patients aged of 61 years [46–73] were included. Median LOD and SAPSII score at ICU admission was of respectively 6 [4–9] and 46 [34–60]. According to our definitions, 67 had no AKI, 54 had pre-renal AKI, and 82 had intrinsic AKI. FeUrea was 39% [28–40%] in the no-AKI group, 41% [29–54%] in the prerenal AKI group, and 32% [22–51%] in the intrinsic-AKI group ($p = 0.12$). FeUrea was of little help for distinguishing prerenal from intrinsic AKI, the area under the ROC curve being 0.59 (95% confidence interval, 0.49–0.70; $p = 0.06$). Sensitivity was 63% and specificity was 54% with a cutoff of 35%. In the subgroup of patients receiving diuretics ($n = 63$), performance of FeUrea were similar (AUC ROC Curve 0.58 [0.41–0.75]).

Of the usual urinary indices, performance was best for the urine/plasma urea ratio (ROC curve AUC, 0.71 [0.62–0.80]). This translates at optimal cut-off (urine/plasma urea ratio less than 12) into a 66% sensitivity and 66% specificity to detect an intrinsic AKI (positive LH, 1.94; and negative LH, 0.52).

**CONCLUSION.** FeUrea may be of little help for separating prerenal from intrinsic AKI in critically ill patients, including those on diuretic therapy. Additional studies are needed to evaluate alternative markers or strategies for differentiating prerenal from intrinsic AKI.

**REFERENCES.** 1. Bagshaw S et al (2007) Intensive Care Med 33:1285–1296

2. Bellomo R et al (2001) Intensive Care Med 27:1685–1688

## 0836

### THE EPIDEMIOLOGY OF CONTRAST- INDUCED ACUTE KIDNEY INJURY IN ICU PATIENTS

S. Doom[1], L. Delrue[1], C. Danneels[1], J. Decruyenaere[1], E. Hoste[1]

[1]Dept of Intensive Care Medicine, University Hospital, Ghent, Belgium

**INTRODUCTION.** Contrast-induced acute kidney injury (CI-AKI) accounts for more than 10% of hospital-acquired AKI and is associated with increased mortality. Diagnostic and interventional procedures with radiocontrast are common in Intensive Care Unit (ICU) patients. Nevertheless, there are little data about the epidemiology of CI-AKI in this group of high risk patients.

**OBJECTIVES.** The aim of this study was to examine the incidence of CI-AKI in ICU patients. We also examined risk factors for CI-AKI and outcomes such as treatment with renal replacement therapy (RRT) within 1 w after contrast, length of stay (LOS) in the ICU, and ICU mortality rate.

**METHODS.** We performed a single-centre, retrospective study in our 56 bed tertiary care ICU. Data were collected from the computerized ICU database during the period 18-03-2004 until 31-12-2008. We included patients who received intravascular iodated radiocontrast during a computed tomography (CT) or a non-coronary angiography procedure during ICU stay. Only the first procedure was evaluated. Patients who had another procedure within 3 days after the first were excluded. We also excluded patients who were treated with RRT at time of procedure. CI-AKI was defined as an increase in serum creatinine (Cr) of $\geq$25% or an increase of $\geq$0.5 mg/dl within 3 days after contrast administration. Contrast media were non-ionic and iso- or low-osmolar.

**RESULTS.** We identified 1,421 ICU patients who underwent a CT with contrast or an angiography. Of these, 619 were excluded, resulting in a study population of 802 patients. CI-AKI occurred in 133 patients (16.6%). These patients were older (65 year vs. 59, $p = 0.004$), more severely ill, as illustrated by a higher APACHE II score (20 vs. 17, $p < 0.001$), worse kidney function at baseline (Cr = 1.17 mg/dl vs. 0.78, $p < 0.001$; lower 24 h urine output 1.4 l vs. 2.2, $p < 0.001$), lower blood pressure (MAP = 65 mmHg vs. 72, $p < 0.001$), a more positive fluid balance preceding contrast (2.3 L vs. 1.1, $p < 0.001$), more often on vasoactive therapy (51.1% vs. 31.1%, $p < 0.001$) and required mechanical ventilation more frequently (63.9% vs. 50.7%, $p = 0.005$). They had more risk factors for development of CI-AKI: drug treatment with diuretics, aminoglycosides, ACEI's, ARB's or NSAID's (43.6% vs. 30.5%, $p = 0.003$), and natriuresis < 20 mmol/l (24.8% vs. 13.3%, $p = 0.001$). The incidence of CI-AKI was comparable in patients who underwent an angiography and a CT (both 16.6%). The incidence of RRT treatment was higher (13.5% vs. 4.2%, $p < 0.001$) in CI-AKI patients; they also had a longer LOS-ICU (17d vs. 11, $p < 0.001$), and higher ICU mortality (35.3% vs. 11.5%, $p < 0.001$). Also after correction for covariates CI-AKI had a strong association with ICU mortality (OR = 3.1, 95% CI = 1.9, 5.1, $p < 0.001$).

**CONCLUSIONS.** CI-AKI occurred in 1 out of 8 ICU patients and was associated with worse outcomes such as need for RRT, and mortality. CI-AKI was a strong predictor for ICU mortality, even after correction for other covariates.

**GRANT ACKNOWLEDGEMENT.** None.

# Impact of technology and drugs in the ICU: 0837–0841

## 0837

### CORRELATION BETWEEN LUNG SOUND HOMOGENEITY INDEX AND STATIC COMPLIANCE: PRELIMINARY FINDINGS

S. Lev[1], M. Shapiro[2], J. Cohen[2], Y. Glickman[3], P. Singer[1]

[1]Rabin Medical Center, Beilinson Hospital, Petach Tiqva, Israel, [2]RMC, Petach Tiqva, Israel, [3]Deep Breeze, Ltd., Or-Akiva, Israel

**INTRODUCTION.** Increased homogeneity of lung sound distribution has been correlated with improved Functional Residual Capacity (FRC) in mechanically ventilated ICU patients. In the present study, we correlate lung sound distribution homogeneity index (HI) with static compliance (Cs).

**OBJECTIVES.** To assess the relationship between lung sound distribution and compliance.

**METHODS.** Thirty-two lung sound measurements were performed with the VRI system in 13 ICU mechanically ventilated patients with lung injury. Patients were recorded at different levels of PEEP before and after recruitment maneuver and Cs was obtained from the ventilator at each data point. HI (range 0–100%) was computed based on the distribution of lung sounds in 4 lung segments at peak inspiration. Cs were compared between two groups (group 1: HI $\leq$ 80% and group 2: HI > 80). *p*-Values were obtained using the Wilcoxon Two Sample Test.

**RESULTS.** Significantly lower static compliance was detected for the group with lower homogeneity index than for the group with higher homogeneity index (31 ml/mbar versus 43 ml/mbar, $p = 0.05$).

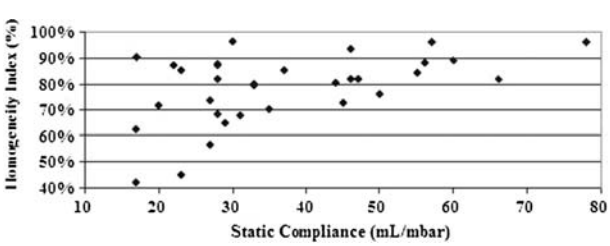


**Fig. 1** Homogeneity index vs static compliance

**CONCLUSION.** Homogeneity of lung sound distribution decreases with decreased lung compliance.

## 0838

### NEW ANTICOAGULATION METHOD WITH SELECTIVE IN-CIRCUIT BLOOD COOLING FOR CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT): THE EFFECT ON PLATELET AND LEUKOCYTE FUNCTION

A. Krouzecky[1], J. Chvojka[1], R. Sykora[1], J. Radej[1], I. Novak[1], J. Ruzicka[2], J. Benes[2], Z. Petrankova[2], J. Hanzlikova[3], L. Bultasova[4], M. Matejovic[1]

[1]Charles University Medical School and Teaching Hospital, ICU, 1st Medical Dept., Plzen, Czech Republic, [2]Charles University Medical School, Dept. of Biophysics, Plzen, Czech Republic, [3]Charles University Medical School and Teaching Hospital, Institute of Immunology and Allergology, Plzen, Czech Republic, [4]Charles University Medical School and Teaching Hospital, Institute of Clinical Biochemistry and Hematology, Plzen, Czech Republic

**INTRODUCTION.** We have recently shown that a selective in-circuit blood cooling (to 20°C) is effective alternative strategy for anticoagulation during 6 h hemofiltration. To further test its safety we investigated the effects of long-term procedure on functional properties of platelets and leukocytes.

**METHODS.** 13 anesthetized and ventilated pigs were randomized to receive continuous hemofiltration (CVVH) with anticoagulation secured either with selective cooling of extracorporeal circuit (ECC) (COOL; $n = 8$) or with standard systemic heparinization (HEPARIN; $n = 5$). Before the procedure (T0) as well as 1, 6 and 24 h after starting the hemofiltration following variables were assessed: 1) agregability of platelets (area under aggregation curve = AUC; velocity of aggregation = VEL); 2) blastic transformation of T-lymphocytes (DNA analysis = DNA) and 3) leukocyte oxidative burst (Bursttest = BURST).

**RESULTS.** Data are median and interquartile range. The median duration of procedure in COOL group was 17 h (6;22), the patency of all circuits treated with systemic heparinization was maintained within the predetermined study period (24 h).

**TABLE 1** FUNCTIONAL PROPERTIES OF PLATELETS AND LEUKOCYTES

| Variable | Group | T0 | T1 | T6 | T24 |
|---|---|---|---|---|---|
| AUC (AU) | COOL | 18.5 (17; 22) | 18 (15.5; 19) | 14 (9; 17) | 12 (6; 15.8) |
| | HEPARIN | 11.5 (9; 19) | 14 (9.5; 18) | 13 (9.3; 15.3) | 16 (13.5; 20.5) |
| VEL | COOL | 5.9 (5.4; 6.1) | 5.3 (4.8; 5.5) | 5 (4.3; 5.3) | 4.4 (3; 5.2) |
| (AU/min) | HEPARIN | 6.1 (4.8; 6.8) | 4.4 (4; 5.1) | 4.2 (3.7; 7.1) | 5 (4.1; 5.6) |
| DNA (%) | COOL | 26.6 (20.2;33.2) | 29.3 (19.8;34.4) | – | 39.8 (33.8;41.7) |
| | HEPARIN | 38 (29;42) | 37 (32;46) | – | 43 (33;47) |
| BURST (%) | COOL | 98 (96;99) | 99 (96;100) | – | 99 (97;100) |
| | HEPARIN | 98 (86;100) | 99 (92;100) | – | 99 (98;100) |

**CONCLUSION.** The method of selective in-circuit blood seems to be effective in maintaining ECC patency for several hours without adversely affecting functional properties of leukocytes and platelets.

**GRANT ACKNOWLEDGEMENT.** MSM 0021620819 Replacement of and support to some vital organs.

**REFERENCE.** Krouzecky et al (2009) Intensive Care Med 35:364–370

## 0839

### FONDAPARINUX VS LOW MOLECULAR WEIGHT HEPARIN AS A THROMBOPROPHYLAXIS IN CRITICALLY ILL PATIENTS. COAGULATION STATUS MONITORED BY THROMBOELASTOGRAPHY (TEG)

G. Mineo[1], N. D. Cascio[1], D. Canzio[1], L. Marino[1], G. Evangelico[1], A. Cortegiani[1], S. M. Raineri[1]

[1]University of Palermo, Anesthesiology and Intensive Care, Palermo, Italy

**INTRODUCTION.** The rationale for use of thromboprophylaxis is based on solid principles and scientific evidence. Almost all hospitalized patients have at least one risk factor for VTE, and approximately 40% have three or more risk factors Without thromboprophylaxis, the incidence of objectively confirmed, hospital-acquired DVT is approximately 10–40% among medical or general surgical patients and 40–60% following major orthopedic surgery. Thromboprophylaxis with unfractionated heparin (UF) or low molecular weight heparins (LMWHs), UTI is often associated to thrombocytopenia, poorly tolerated in critically ill patients. The Fondaparinux (F) is the first of a new class of antithrombotic drugs that selectively inhibits factor Xa, has no direct effect on IIa and it is not associated with a thrombocytopenia. The aim of this study was to monitoring the coagulation status of critically ill patients undergoing therapy with F and LMWH by the thromboelastography (TEG).

**METHODS.** We enrolled 32 patients with COPD, and APACHE II >25. 16 treated with F (2.5 mg/day) (Group F) and 16 with LMWH (Group H). In these patients TEG was performed at the admission and twice daily during hospitalization. Were evaluated the average r, k, MA, and Ly 30.

**RESULTS.** Groups were homogeneous for age, sex and APACHE II. The differences in average time to TEG have shown non-significant in both groups of patients regarding r, k and Ly30. While we found a progressive reduction of MA patients in group H than in group F which is significant in 10th day (Table 1). No thromboembolic or hemorrhagic complication was recorded.

**TABLE 1** TEG PARAMETERS AND PLATELET COUNTS

| | Group F | | | Group H | | |
|---|---|---|---|---|---|---|
| | T0 | T5 | T10 | T0 | T5 | T10 |
| r (min) | 4.9 (1.9) | 5.1 (1.6) | 6.9 (0.9) | 5.3 (1.6) | 5.5 (1.6) | 6.1 (1.2) |
| MA (mm) | 62 (15) | 67 (10) | 61 (13)* | 63 (12) | 54 (15) | 29 (13)* |
| Ly30 (%) | 3.6 (1.2) | 4.4 (1.2) | 4.1 (1.4) | 4.3 (0.3) | 3.9 (1.6) | 4.4 (1.5) |
| PTL (*10.000) | 161 (41) | 153 (41) | 140 (26) | 159 (53) | 141 (58) | 134 (62) |

*$p < 0.05$

**CONCLUSION.** F and LMWH were equally safe. Monitoring by TEG showed a significant reduction in platelet function in Group H than in group F but not in platelet counts. These results suggest that prophylaxis with F is as effective and safer than LMWH in critically ill patients and monitoring dynamic coagulation by TEG is a useful method to evaluate the appropriateness and the timing of invasive procedures.

**REFERENCE.** 1. Cohen AT, Davidson BL, Gallus AS et al (2006) Efficacy and safety of fondaparinux for the prevention of venous thromboembolism in older acute medical patients: randomised placebo controlled trial. BJM 332(7537):325–329

## 0840

### THE EFFECT OF PROMETHEUS© DEVICE ON LABORATORY MARKERS OF INFLAMMATION AND TISSUE REGENERATION IN ACUTE LIVER FAILURE MANAGEMENT

M. Rocen[1], E. Kieslichova[1], D. Merta[1], E. Uchytilova[1], Y. Pavlova[1], P. Trunecka[1]

[1]IKEM, Prague, Czech Republic

**INTRODUCTION.** Prometheus© based on modified FPSA (Fractionated Plasma Separation and Adsorption) method is used in therapy of acute liver failure as a bridge to liver transplantation. Clinical features of acute liver failure are similar to septic shock as well as the dynamics of inflammatory markers level. We suppose, that the therapeutic effect of Prometheus© treatment for patients with liver failure is caused not only by the elimination of terminal metabolites (urea, creatinine, ammonia, bilirubin). The aim of the study was to identify the impact of treatment on the levels of released cytokines and markers of inflammation and liver regeneration.

**METHODS.** From VII/06 till XI/08, 11 consecutive patients on the waiting list for liver transplantation with acute liver failure were investigated. These patients underwent 26 therapeutic courses on Prometheus© device. Before and after each treatment blood samples were drawn and processed by Elisa method on Luminex equipment, the plasma levels of IL-1a, IL-6, IL-8, IL-10, IL-12, TNFα, HGF and α1 fetoprotein were surveyed. PCT was determined by the immunoluminometric assay. Patients were observed and treated conservatively according to their clinical status until transplantation. All data were prospectively recorded to the protocol. Statistic processing: we evaluated the kinetics of cytokines plasmatic concentrations during each treatment procedure by the method of pair *t*-tests and nonparametrics by Mann–Whitney tests.

**RESULTS.** The experimental group consists of 3 males and 8 females, of average age 39.6 ± 12.1 years. Hepatic impairment at the time of FPSA treatment indication was according to Child-Pugh score 12.8 points ± 0.7 (C) and SOFA score 12.6 ± 5.6 before each treatment. Total of 26 courses of FPSA were undertaken (1–8 per patient), on every other day. In the samples drawn prior to the therapy, there were detected elevated levels of IL-6, IL-8,IL-10, TNFα, CRP and PCT. The level of TNFα decreased significantly ($p < 0.05$) during the therapy, the decrease of CRP and PCT was significant ($p < 0.01$), ($p < 0.05$) as well. The level of α1 fetoprotein ($p < 0.01$) also declined significantly during FPSA elimination. Surprisingly an increase of HGF ($p < 0.05$) was detected. The decline in concentrations of IL-6, IL-8, IL-10 was not significant. Serum concentrations of IL-1a and IL-12 were not elevated.

**CONCLUSIONS.** Our results show that Prometheus© is effective in the clearance of inflammatory mediators responsible for SIRS, and that Prometheus© therapy affects the serum levels of inflammatory and regeneration markers important for therapeutic approach in acute liver failure.

**GRANT ACKNOWLEDGEMENT.** Supported by the Research project IGA NR/9405-3 of the Czech Ministry of Health.

## 0841

### CELL DEATH IN ACUTE HEPATIC FAILURE AND MARS TREATMENT

B. A. Lubsczyk[1], G. Roth[1], J. Pilz[1], P. Faybik[1], H. Hetz[1], A. Bacher[1], C. Krenn[1]

[1]Medical University of Vienna, General Hospital, Dept. of Anaesthesia and Intensive Care Medicine, Vienna, Austria

**INTRODUCTION.** Apoptosis and necrosis from hepatocytes are a hallmark of acute hepatic failure. Caspase cleaved cytokeratin 18 (CK18) has been recently identified as a novel apoptosis serum marker for epithelial cells, whereas total CK18 is released when cells undergo necrosis. Serum nucleosomes have been also successfully used as a marker for cell death in a variety of cell types and disease states. Apoptosis from leukocytes as well as hepatocytes has been recently linked to the immune dysfunction seen in patients suffering from acute hepatic failure. Artificial liver assist devices like the molecular adsorbent recirculating system (MARS) have been introduced in clinical practice to support organ function or to bridge to liver transplantation.

**OBJECTIVES.** We sought to investigate, if there are differences regarding apoptosis and necrosis in acute liver failure (ALF) or acute on chronic liver failure (ACLF).Further we studied the effect of the MARS on this cell death markers, since triggering of apoptosis or necrosis by the extracorporeal blood circuit of MARS could have deleterious effects in ALF and ACLF, and mitigate beneficial effects of the MARS treatment.

**METHODS.** Serum concentrations of cleaved CK18, total CK18 and nucleosome levels were determined by a commercially available ELISA kits in ten ALF and ten ACLF patients undergoing MARS immediately before and after the first treatment cycle. Indications for MARS therapy were ammonia levels of 100 μmol/l or higher with hepatic encephalopathy grade 3, eligibility for liver transplantation. 12 patients with chronic hepatic failure (CHF) with Child-Pugh-Score C, who were clinically stable as well as 14 healthy individuals served controls. Data are given as median with range.

**RESULTS.** Baseline cleaved CK-18 serum concentrations were significantly increased in ALF and ACLF patients as compared to the healthy controls ($p < 0.002$ for both). Cleaved CK18 was significantly increased in CHF compared to the healthy controls ($p < 0.01$). Differences between the ALF, ACLF and CHF group did not reach statistical significance. Results for total CK18 were similar. Baseline nucleosome serum concentrations were significantly increased in ALF and ACLF patients as compared to CHF and healthy controls. Between the ALF and ACLF group there was no statistically significant difference. MARS had no obvious effect on the cleaved CK18, total CK18 and nucleosome serum concentrations. In both populations, ALF as well as the ACLF, serum concentrations remained constant

**CONCLUSIONS.** Serum nucleosome levels maybe useful to discern acute from chronic hepatic failure or to monitor the course and the severity of the disease. MARS therapy apparently did not stimulate the production of these cell death related molecules in our patient collective after one treatment cycle, providing no evidence of deleterious effects through increased cell death triggered by MARS.

# Severe infections 2: 0842–0846

## 0842

### IMPACT OF ORAL DECONTAMINATION WITH CHLORHEXIDINE 1% GEL ON COLONISATION OF THE RESPIRATORY TRACT IN VENTILATED PATIENTS IN A GENERAL ICU

R. J. H. Jackson[1], F. E. Kelly[1], W. English[1], J. Gatward[1], T. Gould[1]

[1]Bristol Royal Infirmary, Intensive Care Unit, Bristol, United Kingdom

**INTRODUCTION.** Ventilator associated pneumonia (VAP) is common in critically ill patients, and is associated with increased mortality. Aspiration of bacteria from the oropharynx is thought to be important in the pathogenesis of the condition. Consequently, selective digestive tract decontamination has been used to reduce the oral bacterial load in an attempt to reduce the incidence of VAP, although the efficacy of this remains unclear [1, 2]. Concerns regarding increased selection of antibiotic-resistant bacteria have resulted in a search for alternative strategies to reduce airway contamination. Topical application of the antiseptic chlorhexidine gluconate (CHX) has achieved varying results, however, the concentration and formulation has varied between studies. In cardiac surgical patients at low risk of VAP, CHX 0.12% was effective at reducing VAP [3]. In medical and mixed ICU populations, CHX 0.12% was found to be ineffective in most trials although CHX 2% did show a reduction in VAP [4]. CHX 2% is not available in the UK. CHX 1% gel is used by our oral surgery department, so we introduced this to our ICU and audited the results.

**OBJECTIVES.** To assess the impact of routine oral CHX 1% gel application on culture rates from bronchoalveolar lavage (BAL) and protected catheter (PC) screening performed on ventilated patients in a 14-bed medical and surgical ICU in a University Hospital.

**METHODS.** Permission was obtained from our clinical audit department. Data were collected retrospectively for all BAL and PC samples for two consecutive 6-month periods: before and after the implementation of routine CHX oral decontamination (in January 2008). PC samples were collected routinely for screening on a twice weekly basis, and BAL was performed when clinically indicated. PC samples were considered positive if $>10^4$ colony forming units (CFU) were present; BAL if $>10^5$ CFU were present. Where a sample grew multiple organisms, this was considered as a single positive result.

**RESULTS.** Prior to CHX use, 154 samples (20 BAL, 134 PC) were collected. Of these 24 (15.6%, 3 BAL, 21 PC) were positive. Following commencement of routine CHX use, 225 samples (71 BAL, 154 PC) were collected. Of these, 19 (8.4%, 4 BAL, 15 PC) were positive. The reduction in positive results was statistically significant (2-sided Fisher's exact test, $p = 0.047$). CHX appeared to exhibit greatest impact on gram-negative organisms (23 positive cultures pre-CHX, 13 post-CHX), whilst having the opposite effect upon fungi (3 positive cultures pre-CHX, 6 post-CHX).

**CONCLUSIONS.** In this small retrospective study, a reduction in the rate of microbiological contamination of the lower respiratory tract was observed following the introduction of routine oral decontamination with CHX 1% gel in invasively ventilated patients. No adverse incidents involving CHX were reported during the study period.

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**GRANTS.** None.

## 0843

### ANTIBIOTIC PRESCRIBING HABITS IN A TERTIARY REFERRAL INTENSIVE CARE UNIT

D. Trainor[1], S. Gallagher[1], L. James[1], P. Glover[1]

[1]The Regional Intensive Care Unit, The Royal Victoria Hospital, Belfast, United Kingdom

**INTRODUCTION.** More than 75% of patients admitted to the intensive care unit (ICU) receive at least one antibiotic during their stay [1]. In patients suffering from severe sepsis and septic shock prompt antimicrobial therapy saves lives [2]. However, it has been recognised that excessive and inappropriate use of antibiotics is associated with the emergence of multidrug resistant bacteria [3].

**OBJECTIVES.** We carried out a prospective observational study of antibiotic prescribing habits in 30 consecutive patients admitted to a tertiary referral mixed medical-surgical adult ICU.

**METHODS.** We examined antibiotic prescriptions prior to ICU admission, prescriptions initiated in ICU, whether prescriptions were empirical or targeted against identified organisms, and duration of antibiotic prescribing. Microbiological results and the impact this had on antibiotic prescriptions were also noted.

**RESULTS.** Twenty-four (80%) patients received at least one antibiotic during their ICU stay (median length of stay (LOS) 6 days). Six patients (20%) did not receive any antibiotics whilst in ICU (median LOS 1.5 days). Antibiotics were prescribed prior to ICU admission in 37% of patients, but only 30% of these prescriptions were continued in ICU. Pneumonia was the commonest indication for antibiotics that were commenced on the ward (87%) and continued in ICU. 63% of antibiotic administrations commenced in ICU were empirical (mean duration 3.4 days), 34% targeted (mean duration 9.8 days) and 3% prophylactic (single dose). Empirical antibiotic prescriptions commenced in ICU were discontinued within 24 h in 33% of cases. Administration of antibiotics occurred within 30 min of the initial prescription in 55% of cases. No positive microbiological results were obtained in 54% of patients who received antibiotics in ICU. Staphylococcus aureus was the commonest organism identified in cases of suspected pneumonia. This was MRSA in 3 out of 4 cases.

**CONCLUSIONS.** Increasing duration of ICU stay is associated with a greater risk of receiving antibiotics. Antibiotics are often prescribed in the absence of positive microbiological results. Most patients receiving antibiotics within our ICU initially received empirical antibiotics, which were administered for a shorter time than targeted antibiotics. It could be argued that the development of techniques to confirm the presence of bacterial infection may reduce inappropriate antibiotic administration. These measures may help to decrease the development of multiresistant bacteria and reduce drug prescribing costs.

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## 0844

### REDUCING METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) TRANSMISSION AND BACTERAEMIA IN INTENSIVE CARE: IMPACT OF UNSELECTIVE DECOLONISATION IN ADDITION TO STANDARD MEASURES

N. T. Tarmey[1], A. P. Pallett[2], J. M. B. Fennell[1]

[1]Southampton General Hospital, General Intensive Care Unit, Southampton, United Kingdom, [2]Southampton General Hospital, Microbiology Department, Southampton, United Kingdom

**INTRODUCTION.** Methicillin-resistant Staphylococcus aureus (MRSA) is a worldwide cause of morbidity and mortality in the intensive care unit (ICU) [1]. Current recommendations include active surveillance, improved antibiotic stewardship and the general principles of infection control [2]. It has also been suggested that unselective decolonisation may be effective for the control of MRSA propagation when other measures have failed [3]. We present our experience of reducing MRSA bacteraemia in the ICU by a series of measures, including unselective decolonisation of all patients admitted to the unit.

**OBJECTIVES.** To examine the effectiveness of a series of interventions to reduce MRSA transmission and bacteraemia in the ICU.

**METHODS.** In April 2005, detailed data collection began for all cases of MRSA in our institution, a mixed medical and surgical ICU. Between April and December 2005, MRSA control measures included: active surveillance with isolation of carriers; reduced cephalosporin and fluoroquinolone usage; improved environmental cleaning; hand hygiene and infection control training for staff; chlorhexidine 4% wash for carriers and contacts. In February 2006, unselective decolonisation of all patients was begun. All ICU admissions received chlorhexidine 4% wash, once daily for 5 days and mupirocin 2% nasal ointment, three times daily for 5 days.

**RESULTS.** During the first 12 months studied (April 2005–March 2006 inclusive), 51 patients were admitted to ICU colonised with MRSA, 31 patients became MRSA colonised in ICU and there were 15 cases of MRSA bacteraemia in ICU. During the last 12 months studied (January 2008–December 2008 inclusive), 74 patients were admitted to ICU colonised with MRSA (an increase of 45%), 3 patients became MRSA colonised in ICU (a reduction of 90%) and there was 1 case of MRSA bacteraemia (a reduction of 93%). Mupirocin resistance was not detected in any samples from ICU during the period studied.

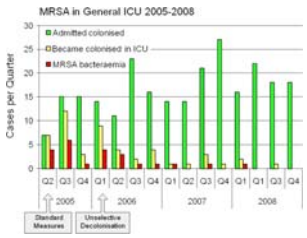


**Fig. 1** MRSA in General ICU 2005–2008

**CONCLUSIONS.** The measures taken were effective in reducing MRSA transmission by 90% and in reducing MRSA bacteraemia by 93% in ICU. This was in spite of an increase in the number of patients admitted to the ICU colonized with MRSA. Unselective decolonisation with 4% chlorhexidine washes and nasal mupirocin appears to have contributed significantly to this effect.

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**GRANT ACKNOWLEDGEMENT.** None

## 0845

### IDENTIFYING SEPSIS IN TRIAGE: ASSESSMENT OF A NURSE TRIAGE TOOL

C. Cleophax[1], S. Bernard[2], V. Pasquereau[2], M. Celine[3], L. Poiree[4], N. Simon[2]

[1]Poissy Hospital, Intensive Care Unit, Poissy, France, [2]Poissy Hospital, Poissy, France, [3]Meulan Hospital, Meulan, France, [4]Neuilly Hospital, Neuilly sur Seine, France

**BACKGROUND.** International guidelines highlight the necessity of early identification of severe sepsis. Triage procedures in the emergency department (ED) represent the first step in the sepsis chain of survival.

**OBJECTIVES.** This study assessed a tool intended for the triage nurse to correctly identify actual or impending severe sepsis.

**METHODS.** A prospective study was done in three ED, during 2 months. A specific sepsis triage aid was used for the identification of a possible sepsis syndrome and for risk factors of impending or obvious severity. The sepsis syndromes were ultimately confirmed and classified by the emergency physician. Final diagnosis was compared with the initial triage.

**RESULTS.** Among the 253 patients eventually diagnosed with sepsis, 205 were correctly identified by the triage nurse. The calculated triage sensitivity was 81% [95% CI: 76–85] for identification of sepsis and 75% [95% CI: 64–85] for correct prioritization of severe sepsis.

**DISCUSSION.** Some patients did not present initially with clinical criteria of sepsis and deteriorated during their stay in the ED. Most of non-suspected patients with sepsis had not been correctly screened. Furthermore time necessary to apply the screening procedure often seemed too long in the setting of triage.

**CONCLUSION.** A simple triage aid for sepsis seems promising. Such a tool must use simple but relevant criteria and consider the rapid change in clinical state in potentially septic patients.

### 0846

**FLUID LEAKAGE PAST TRACHEAL TUBE CUFFS: EFFECT OF SUCTIONING MANOEUVRE AND TYPE OF CUFF IN A BENCHTOP MODEL**

P. Beuret[1], M.-J. Carton[1], M. Kaaki[1], X. Fabre[1], J.-C. Ducreux[1]

[1]Centre Hospitalier, Intensive Care Unit, Roanne, France

**INTRODUCTION.** The leakage of oropharyngeal secretions around tracheal tube cuffs is usually considered as a major risk factor for bacterial tracheal colonization. Tracheal suctioning enhances leakage, by decreasing tracheal pressure. This study aimed to evaluate the effect of a suctioning manoeuvre without disconnection of the ventilator on leakage, according to the modalities of suctioning and the type of cuff.

**METHODS.** A benchtop model of trachea was created using a plastic tubing whose diameter was in the range of an adult trachea (antero-posterior ID 24 mm, transversal ID 20 mm). The trachea, angled at 30°, was intubated with a size 7.5 mm ID tracheal tube whose proximal end was connected to a mechanical ventilator—Servo i (Siemens); the distal end of the trachea was connected to a test lung (Siemens). The ventilator settings were as follows: volume-control mode, respiratory rate 12 bpm, peak inspiratory pressure at 20 cm H2O, PEEP at 5 cm H2O. The cuff pressure was set at 30 cm H2O. Then, 0.5 ml blue dye followed by 3 ml saline was instilled just above the cuff. Three types of tubes were tested: Hi-Lo Evac (Mallinckrodt) with polyvinyl chloride cuff, Microcuff (Kimberly-Clark) and Sealguard (Mallinckrodt) with polyurethane cuffs. For each type of tube, leakage of dye was evaluated with each of three sizes of suction catheter (12-14-16 French) and three levels of suction pressure (−100, −200, −400 cm $H_2O$). Suctioning was performed hourly along 8 h. Each experiment was performed five times.

**RESULTS.** Once the cuffs were inflated to a pressure of 30 cm H20 in the model of trachea, longitudinal folds were observed within the cuff wall of Hi-Lo Evac and Sealguard tubes, but none for Microcuff**.** During baseline ventilation with PEEP without suctioning, no leakage was observed along 8 h with the three types of tube. The incidence of leakage during suctioning is detailed in Table 1.

**TABLE 1**

| Tracheal tube | Negative pressure (cm $H_2O$) | Suction catheter size (French) | Leakage |
|---|---|---|---|
| Hi-Lo Evac | −400 | 16-14-12 | 5/5-5/5-1/5 |
| | −200 | 16-14-12 | 5/5-5/5-0/5 |
| | −100 | 16-14-12 | 0/5-0/5-0/5 |
| Sealguard | −400 | 16-14-12 | 1/5-0/5-0/5 |
| | −200 | 16-14-12 | 1/5-0/5-0/5 |
| | −100 | 16-14-12 | 0/5-0/5-0/5 |
| Microcuff | −400 | 16-14-12 | 0/5-0/5-0/5 |
| | −200 | 16-14-12 | 0/5-0/5-0/5 |
| | −100 | 16-14-12 | 0/5-0/5-0/5 |

**CONCLUSION.** In this model, no leakage of fluid was observed past the three types of tube tested during 8 h of volume-controlled ventilation with a PEEP level at 5 cm $H_2O$. During suctioning, when using low levels of negative pressure no leakage was observed with the three tubes tested. When using high levels of negative pressure, the Microcuff was the sole tube allowing the use of large size catheters without leakage.

## Paediatrics: 0847–0851

### 0847

**SINGLE NUCLEOTIDE POLYMORPHISMS (SNP'S) IN GENES OF CIRCULATORY HOMEOSTASIS IN SURVIVING PEDIATRIC INTENSIVE CARE PATIENTS WITH MENINGOCOCCAL INFECTION**

H. E. Bunker-Wiersma[1], R. P. Koopmans[2], T. W. Kuijpers[1], H. Knoester[1], A. P. Bos[1]

[1]Emma Childrens Hospital/AMC, Pediatric Intensive Care Unit, Amsterdam, Netherlands, [2]AMC, Clinical Pharmacology and Pharmacotherapeutics, Amsterdam, Netherlands

**OBJECTIVE.** In the course of a meningococcal infection, invasive and severe disease occurs in a restricted number of individuals. The predominant mechanism of death in case of meningococcal septic shock is circulatory failure. Inotropic requirements between patients vary widely. We investigated whether polymorphisms in genes regulating the hemodynamic response, influence the amount of inotropics required or the susceptibility to severe meningococcal disease.

**METHODS.** In this retrospective case control study in our Pediatric Intensive Care Unit 56 cases (all consecutive patients admitted to the PICU between 1993 and 2001 with a proven meningococcal infection) and 136 controls were included. Patients were divided in two groups, according to their inotropic requirements. DNA analysis was performed to determine the polymorphisms of the ADRB-1, ADRB2, alpha-adducin, ACE and ATR-1 genes.

**RESULTS.** For the alpha-adducin gene a significant difference of the genotype distribution was found between the cases and controls. The odds ratio for admission to the PICU with meningococcal sepsis with or without meningitis, for carriers of the variant allele (Gly460Trp or Trp460Trp) was 2.1 (95% CI 1.11–4.04; $p < 0.02$). Cases homozygote for the wild type allele of the beta-1 adrenergic receptor at locus 389, were more likely to have a low prism score on admission (OR 3.6 (95% CI 1.11–11.76). No difference was found in the distribution of the ADRB-1, ADRB-2, ACE and ATR-1 polymorphisms between the two groups of patients or between cases and controls.

**CONCLUSIONS.** Among patients admitted to the PICU with a meningococcal infection, the variant allele of the alpha-adducin gene was more prevalent compared to controls. Patients with the variant allele of the ADRB-1 at locus 389 were more likely to have a high PRISM score on admission. In studies in adults the variant allele was associated with decreased renin activity posing a possible explanation for our finding. Measuring plasma renin activity, AT I, AT II, aldosteron synthesis and related polymorphisms will elucidate our hypothesis.

We did not find a difference in the frequencies of polymorphisms from the adrenergic receptor genes, the ATR-1 gene or the ACE (I/D) polymorphism between cases and controls while others found an increased mortality among carriers of the ACE D-allele in a comparable population. We did not have access to the DNA of the deceased patients, which may have influenced our results.

### 0848

**LOW CD8 T-CELLS IN NEONATES AND INFANTS PRIOR TO SURGERY AND HEALTHCARE-ASSOCIATED INFECTIONS: A PROSPECTIVE OBSERVATIONAL STUDY**

S. Grosek[1], Z. Petrin[2], A.N. Kopitar[3], J. Grosek[4], J. Erzen[5], T. Stopar Gmeiner[6], M. Petreska[1], J. Primozic[1], A. Ihan[3]

[1]University Medical Centre Ljubljana, Department of Pediatric Surgery and Intensive Care, Ljubljana, Slovenia, [2]Department for Intensive Care Medicine, University Medical Center Ljubljana, Ljubljana, Slovenia, [3]Medical Faculty, University of Ljubljana, Institute of Microbiology and Immunology, Ljubljana, Slovenia, [4]University Medical Centre Ljubljana, Department of Abdominal Surgery, Ljubljana, Slovenia, [5]University Medical Centre Ljubljana, Department of Thoracic Surgery, Ljubljana, Slovenia, [6]University Medical Centre Ljubljana, Department for Nuclear Medicine, Ljubljana, Slovenia

**INTRODUCTION.** Major surgery suppresses the cell-mediated immune response in adults and children. Both; innate (HLA-DR monocytes/macrophages, NK cells) and adaptive cell-mediated immune responses (T-cell populations) are affected following major surgery or trauma. Cytotoxic T-cell lymphocytes (CD8 T-cells) fall significantly in neonates postoperatively, while predominantly helper T-cell lymphocytes (CD4 T-cells) are decreased in adult patients and children. Low CD4 T-cell counts and an imbalance between their Th1/Th2 subsets in adult patients following major surgery or trauma were associated with septic complications.

**OBJECTIVES.** Data about preoperative and postoperative counts of T-cell populations in paediatric surgical patients and its relationship to healthcare-associated infection, HAI, are not yet known.

**METHODS.** We conducted a prospective observational study on T-cell populations in peripheral blood, immediately before and after, and in the first 3 days after surgery in 28 children (13 neonates and 15 infants) and their relationship to healthcare-associated infection. Healthcare-associated infections were classified according to CDC/NHSN criteria. The study was approved by the Slovenian Ethics Committee, and informed consent was obtained. The study was conducted in the Level III Multidisciplinary Neonatal and Paediatric Intensive Care Unit in the Department of Paediatric Surgery and Intensive Care, University Medical Centre Ljubljana, Slovenia. During the study period, from January 2007 to May 2008, 28 out of 33 children were included. Thirteen of the children were neonates, with a median (interquartile ranges, IQR) age of 0 (0–2) days, and fifteen were infants, with a median (IQR) age of 5 (2.5–15.5) months.

**RESULTS.** Six out of 28 (21.4%) neonates and infants developed healthcare-associated infection (Group I-HAI), while 22 out of 28 (78.6%) remained infection free (Group II-nonHAI). No differences were found between the two groups with regard to age, weight, gender, blood transfusion, anaesthetic technique and Oxford stress surgical score index. In Group I with HAI presurgical median values of CD8-T-cells were found to be below normal values for age. In addition, we found that median values (M) and interquartile ranges (IQR) of cytotoxic CD8 T-cells were twice as low (358; 304–424 cells/mikrol) compared to Group II withot HAI (822; 522–933 cells/microl; ($p = 0.013$)), while median values of CD8 T-cells in Group I-HAI remained very low throughout the study period.

**CONCLUSIONS.** These results demonstrate that neonates and infants who underwent a major surgical procedure and had very low values of CD8 T-cells preoperatively, developed HAI postoperatively.

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### 0849

**ACCURACY OF THE BROSELOW TAPE, PALS FORMULA, MODIFIED PALS FORMULA, FAMILY MEMBER ESTIMATION AND THE PERCENTILE 50TH OF THE NATIONAL WEIGHT–HEIGHT CORRELATION GRAPH FOR THAI CHILDREN'S WEIGHT ESTIMATION**

S. Trakulsrichai[1], C. Boonsri[1], P. Chatchaipun[2]

[1]Ramathibodi Hospital Medical School, Emergency Department, Bangkok, Thailand, [2]Ramathibodi Hospital Medical School, Section for Clinical Epidemiology and Biostatistics, Research Center, Bangkok, Thailand

**INTRODUCTION.** Accurate children's weight estimation is important for emergency care, particularly for drug dosages, electrical therapy or equipment sizes. Weight is difficult to measure in critically ill children. Several formulae or methods have been developed to estimate children's weight accurately. Most formulae or methods were developed from western countries. The formulae or methods currently used might not fit with Thai children.

**OBJECTIVES.** To determine the accuracy of the Broselow tape, PALS formula, modified PALS formula, family member estimation and the percentile 50th of the national weight–height correlation graph for Thai children's weight estimation.

**METHODS.** The author carried out a prospective cross-sectional study. Children from neonate to 12 years old who presented to the emergency room and general out-patient pediatric clinic were included. The patients were studied in both overall and subgroup analysis (less than 10 kg, 10–25 kg, 25–40 kg and over 40 kg). The primary outcome was the agreement within 10% of the measured weight and the mean difference.

**RESULTS.** 595 patients were included in this study. There were 333 (55.97%) boys and 262 (44.03%) girls. Family member estimation was the most accurate method with 85.21% agreement within 10% of the measured weight and had the lowest mean difference (−0.26 kg). Family members can estimate weight statistically and significantly accurate for all weight subgroups. The Broselow tape was the most accurate method of other alternative methods with 56.13% agreement within 10% of the measured weight and the lowest mean difference (−0.49 kg). The Broselow tape had the best estimation in the weight subgroup less than 10 kg. The agreement within 10% of the measured weight of the percentile 50th of the national weight–height correlation graph were 51.43% and the mean difference were −0.64 kg. The agreement within 10% of the measured weight of PALS and modified PALS formulae were 38.99% and 39.55% respectively. The mean difference of PALS and modified PALS formulae were −0.72 and −0.73 kg respectively.

**CONCLUSIONS.** Family member estimation of weight was the most accurate method in this study. In cases of family member estimation not being available, the Broselow tape was the most accurate alternative method however it could not estimate more than one-third of Thai children accurately.

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## 0850

### GLUCOSE PARAMETERS, GLUCOSE VARIABILITY AND TARGET BLOOD GLUCOSE IN PEDIATRIC TRAUMA PATIENTS

P. Durdik[1], S. Nosal[1], V. Zolak[2], M. Fedor[2], J. Buchanec[3], P. Banovcin[3]

[1]Jessenius Faculty of Medicine Comenius University, Pediatric Intensive Care Unit, Martin, Slovakia, [2]University Hospital Martin, Pediatric Intensive Care Unit, Martin, Slovakia, [3]Jessenius Faculty of Medicine Comenius University, Department of Children and Adolescents, Martin, Slovakia

**OBJECTIVES.** Diabetes of injury with increased serum glucose levels has been associated with higher mortality and poor outcome in severely injured children. Peak blood glucose (BG), duration and intensity of hyperglycemia are independently associated with mortality in PICU (Srinivasan 2004). Strict glucose control by intensive insulin therapy is beneficial. However, higher frequency of severe hypoglycemia and positive metabolic effects of glucose have to be mentioned. The aim of this study is to compare applicability of glucose parameters and glucose variability in pediatric trauma patients and establish target BG in severely injured children.

**METHODS.** prospective clinical study in 2008. 51 children, non diabetic, with Injury Severity Score more than 15 and Pediatric Trauma Score less than 9 points were included. Average age was 9.8 years (6.9–11.9, CI 95%). The mortality showed 13.7%. BG was measured every 3 h by standard biochemical laboratory tests and compared with glucose levels by daily calibrated glucometer. Pediatric scoring systems, predict death rate (PDR) and parameters of hospitalization were collected. Peak BG and glucose intensity were used glucose parameters. The hyperglycemic index, hypo/hyperglycemia ratio and hyperglycemic difference described glucose variability. The nonparametric statistic methods (Spearman correlation and Mann Whitney U test) were used for analysis.

**RESULTS.** Hyperglycemia over 110 mg/dl [6.1 mmol/l] was in 87.3% patients. Both calculated glucose parameter did not show significant difference between survivals and nonsurvivals. All parameters of glucose variability were significantly higher in nonsurvivals ($p < 0.01$). Positive statistical significant correlation between peak BG and PDR3 (Spearman coefficient $r = 0.661$, $p < 0.01$). Target BG in pediatric trauma patients was established from peak BG and PDR3 correlation by using a linear regression analysis. 137 mg/l [7.6 mmol/l] was calculated as optimal BG for risk of mortality lower than 15%.

**CONCLUSION.** Hyperglycemia is very common in injured children. Glucose variability better reflects the outcome and prognosis in pediatric trauma patients. Higher difference of glucose variability has been associated with higher mortality and severe organ failure. Calculated target BG is higher than normal glucose level thus could reflect positive metabolic effect of glucose in injured children and minimize severe hypoglycemic episodes.

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## 0851

### RISK FACTORS OF DEATH IN SEVERE RESPIRATORY SYNCYTIAL VIRUS INFECTION

A. Chakroun Bouziri[1], A. Khaldi[1], A. Hamdi[1], A. Bezzine[1], S. Bel Hadj[1], K. Menif[1], N. Ben Jaballah[1]

[1]Children's Hospital of Tunis, Pediatric Intensive Care Unit, Tunis, Tunisia

**OBJECTIVE.** Respiratory syncytial virus (RSV) has been found to be the most common viral cause of death in children less than 1 year old. The purpose of this study was to determine the mortality rate and the risk factors for death in children with severe RSV infection.

**METHODS.** Retrospective review of the medical records of all children managed in a tertiary pediatric intensive care unit (PICU) for severe RSV infection over a period of 9 years (2000–2008). Need for mechanical ventilation (MV) or non invasive ventilatory support was used as a marker of severity. To determine risk factors for death, a univariate then a multivariate analysis using a logistic regression model were performed.

**RESULTS.** During the study period, 142 patients (median age: 1, 4 months; interquartile range (IQR): 0, 85–2, 4 months) had a severe RSV infection accounting for 3, 8% of total admissions in the PICU and 84% of children managed for RSV infection. Of them 89, 5% required MV and 10, 5% required non invasive respiratory support. Twelve children died (median age: 2 months [IQR 0, 9–5, 1], median length of PICU stay: 17 days [IQR 8–34, 7]) and 130 survived (median age: 1, 4 months [IQR 0, 8–2, 4], median length of PICU stay: 9 days [IQR 5–16]). The overall PICU RSV mortality was 8, 4%. Death was caused by refractory hypoxemia in 4 cases and refractory septic shock in 8 cases. All of the RSV deaths had pre-existing or underlying medical conditions (prematurity: 5 cases, antecedent of neonatal respiratory distress: 5 cases requiring MV in 4 cases, chronic lung disease: 3 cases, cardiac lesions: 3 cases, neuromuscular disease: 1 case) and 7 of them (58, 3%) were hypotrophic. Risk factors for death in univariate analysis were: antecedent of neonatal respiratory distress (41.7% vs 12.3%; $p = 0.017$), antecedent of MV during the neonatal period (33.3% vs 3.8%; $p = 0.003$), occurrence of pulmonary air leak (33, 3% vs 5, 4%; $p = 0.007$), occurrence of nosocomial infection (66.7% vs 20%; $p = 0.001$), prolonged MV (19.9 $\pm$ 14.6 vs 8.6 $\pm$ 6.9 days; $p = 0.000$) and prolonged length of stay (21 $\pm$ 15,8 vs 11.6 $\pm$ 11.5 days; $p = 0.009$). Independent risk factors for death were: antecedent of MV during the neonatal period (OR = 16, 9; 95% CI [2, 7–104]); prolonged MV in the PICU (OR = 12, 1; 95% CI [1, 6–87]) and the occurrence of pulmonary air leak (OR = 9; 95% CI [1, 5–52]).

**CONCLUSIONS.** The mortality rate of severe RSV infection was 8, 4% in our PICU. Antecedent of MV during the neonatal period; prolonged MV in the PICU and the occurrence of pulmonary air leak are associated with a significantly higher risk of death from severe RSV infection.